Name: _____

Chem 633: Advanced Organic Chemistry 2013 ⋯ Midterm

Please answer the following questions *clearly and concisely*. In general, use pictures and less than 10 words in your answers.

Write your answers in the space provided.

Write your initials on each page you want graded.

There are 12 total pages to this exam. The last 2 pages were intentionally left blank and may be used for scratch paper. Please be sure your copy has 12 pages before you begin.
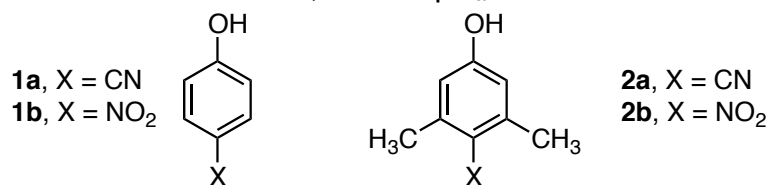
Molecular models are allowed.

Calculators are unnecessary and prohibited.

Problem	Points
1	_____/20
2	_____/30
3	_____/15
4	_____/20
5	_____/15
TOTAL	_____/100

1. (20 points) Please explain the following observations. (Use pictures and few words.)

(a) The pK$_a$ of **1a** and **2a** are the same, but the pK$_a$ of **1b** is much lower than that of **2b**.

1a, X = CN
1b, X = NO$_2$

OH

H$_3$C   CH$_3$
        X

OH

X

2a, X = CN
2b, X = NO$_2$

(b) The gauche conformation of the following molecule is favored over the anti conformation.
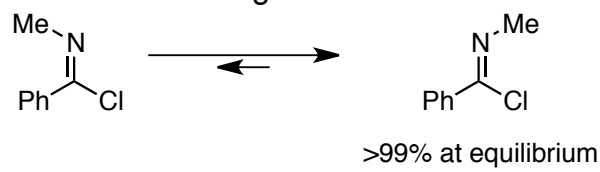
Me^{O}^{O}Me

anti

Me^{O}^{O}

Me

gauche
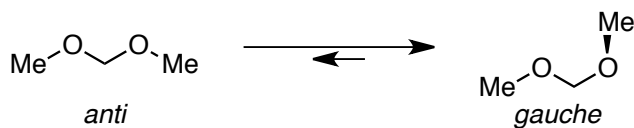
(1 – continued)

(c) The more stable conformation of this tetraaza-cyclohexane has the methyls arranged as shown in **3b**.

Me,,,N⌒N,,,Me / Me N⌒N Me
Me N⌒N Me ⇌ Me N⌒N,,,Me

3a   **3b**
            favored
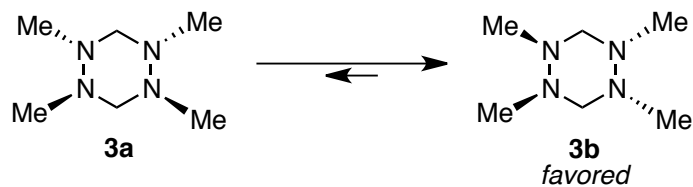
(d) The following equilibrium lies to the right.

Me‑N=C(Ph)(Cl) ⇌ N(Me)=C(Ph)(Cl)

>99% at equilibrium

2. (30 points) The reaction of carbene **1** and aldehyde **A** leads to epoxide **2**. This reaction is rapid and reversible.

1

Aa, R = p-(NO$_2$)C$_6$H$_4$
Ab, R = t-Bu

2a, R = p-(NO$_2$)C$_6$H$_4$
2b, R = t-Bu
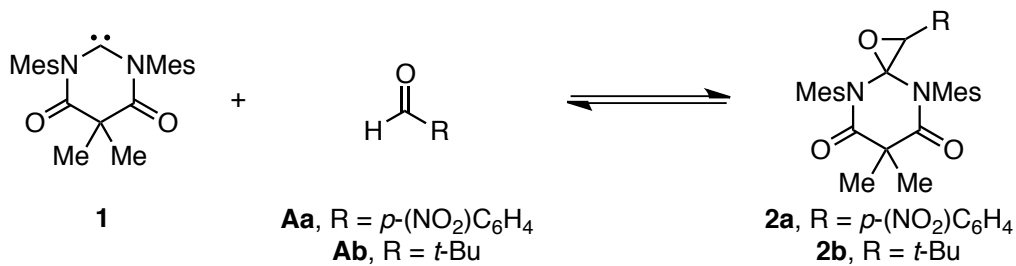
(a) The reaction of aldehyde **Aa** leads to quantitative conversion of the starting materials to the product. Estimate K_{eq} and $\Delta G°$ for this reaction.

(2 – continued)

(b) The reaction of aldehyde **Ab** proceeds to less than 85% conversion. To study this reaction, researchers performed experiments and obtained the following data. Please show how you would determine ΔG° from this data. (Note: You do not need to calculate ΔG°. Just show the equations and how you would plug in the numbers.)
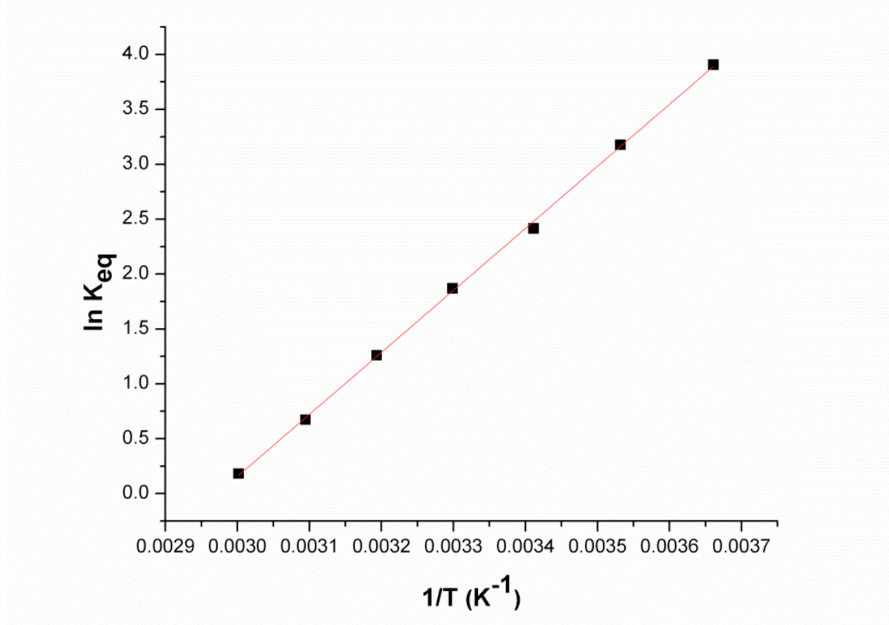

Figure S1. Plot of ln K_{eq} vs 1/T for the reaction **1** + pivaldehyde → **2h**. The equation for the best fit line shown in red is as follows: y = mx + b, where m = 5650 ± 60 K and b = -16.8 ± 0.2.

(2 – continued)

(c) Researchers also wanted to determine $\Delta G^{\ddagger}$, but the reaction was too fast. Instead, they studied the rate of exchange of aldehyde with epoxide **2a**. For these experiments, they used a labeled aldehyde **Aa*** (labeled at **H***) and observed the decay of [**Aa***] and growth of [**2a***]. They hypothesize that this exchange reaction proceeds via **1**.
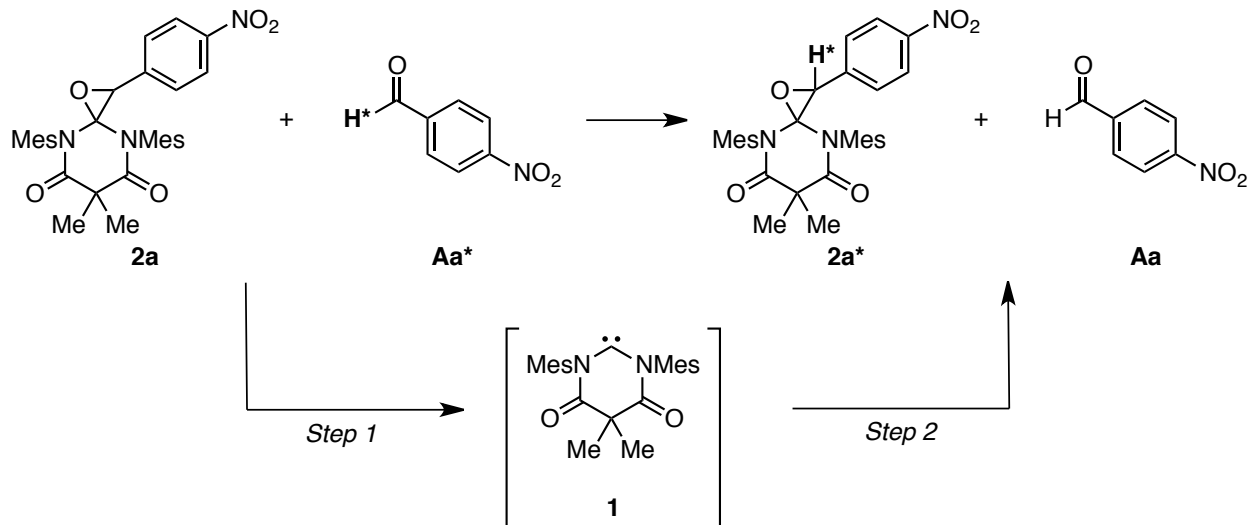
What do the following data tell you?

Entry	Equiv of **Aa***	k_{obs} (s^{-1})
1	4	4.0 ± 0.6
2	2	4.4 ± 0.5
3	1	4.3 ± 0.4

(d) What do the following data tell you?

$\Delta H^{\ddagger} = 23.9 \pm 1.9$ kcal/mol
$\Delta S^{\ddagger} = 8 \pm 5$ cal/mol·K

(2 – continued)

(e) Based on the above data, which step is rate determining (Step 1 or Step 2)?

(f) Please draw a reaction coordinate diagram for the exchange reaction.

3. (15 points) Hydroxyl groups (OH) can be used to direct epoxidations with *m*-CPBA, as shown in transition state **A** below. The epoxidation step is irreversible.

1   (*m*-CPBA, R = *m*-ClC₆H₄)   **A**
transition state   **B**
intermediate   **2**
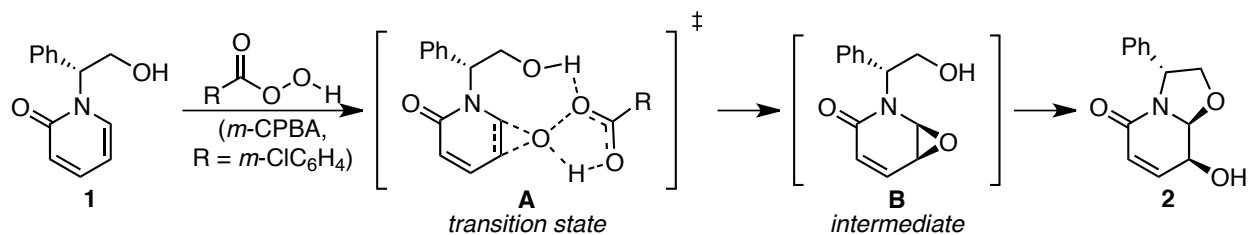
(a) Please explain the observed stereochemistry of intermediate **B**. In other words, why is the epoxide "up"? Include clear, 3-dimensional depictions of transition state **A** in your answer.

(b) Draw a reasonable arrow-pushing mechanism for the transformation of intermediate **B** to product **2** that is consistent with the observed stereochemistry of product **2**.

4. (20 points) The identity of R has a large effect on the rate of the rearrangement shown below. When R = *t*-Bu, the reaction is 370 times faster than when R = H.

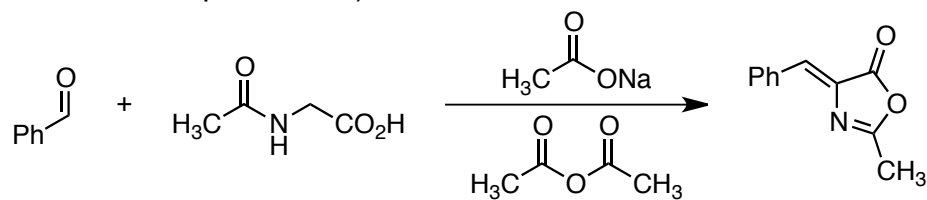| substituent	relative rate
R = H	1
R = *t*-Bu	370
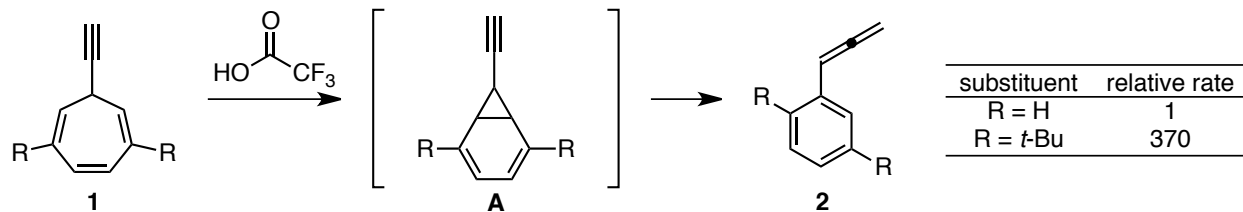
(a) Please explain this rate difference.

(b) Please draw a reasonable arrow-pushing mechanism for the conversion of intermediate **A** to **2**. For each step, please name the HOMO-LUMO interaction(s). You do not need to draw the HOMO or LUMO.

5. (15 points) Please draw a reasonable arrow-pushing mechanism for the following reaction (Grossman, Chapter 2, #2h).

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